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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF APPEALS AND INTERFERENCES

In Re Application of:)
Dilip K. Nakhasi)
Roger L. Daniels)
)
Serial No.: 10/795,843)
Filed: March 8, 2004)
)
For:)
STRUCTURED LIPID)
CONTAINING COMPOSITIONS)
AND METHODS WITH HEALTH)
AND NUTRITION PROMOTING)
CHARACTERISTICS)
)
Examiner: Carolyn A. Paden)
)
Art Unit: 1761)
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APPEAL BRIEF UNDER 37 C.F.R. § 41.37

Raymond M. Mehler
Attorney for Appellants

COOK ALEX LTD.
200 West Adams Street
Suite 2850
Chicago, Illinois 60606
(312) 236-8500

Customer No. 26568

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TABLE OF CONTENTS

i. STATEMENT OF REAL PARTY IN INTEREST 5

ii. STATEMENT OF RELATED APPEALS AND INTERFERENCES.....5

iii. STATUS OF CLAIMS..... 5

iv. STATUS OF AMENDMENTS 5

v. SUMMARY OF CLAIMED SUBJECT MATTER..... 7

vi. GROUNDS OF REJECTION TO BE REVIEWED 10

vii. ARGUMENT 10

THE REJECTION OF THE CLAIMS UNDER 35 U.S.C. §103 SHOULD BE REVERSED 10

A. The Law Regarding Obviousness 10

B. Claims Unobvious: The Multiple References Do Not Disclose All the Claimed Elements 12

1. Claim 1 and its dependent Claims 2-5, 9, 11-13, 20-25, 27 and 29.....12

(a) Aoyama and Product Claim 1 13

(b) Aoyama and "a chemical synthesis" 14

(c) The Secondary References 20

(d) Appellants' Invention is Unobvious ... .24

2. Claim 15 (Dependent on Claim 1) 24

3. Claim 16 (Dependent on Claim 1) 25

4. Claim 17 (Dependent on Claim 1) 26

5. Claim 37 (Independent).....27

6. Independent Claim 40 and its Dependent Claims 41, 43, 44 and 46 28

7. Claim 47 (Dependent on Claim 40) 29

8. Claim 48 (Dependent on Claim 40) 30

C. Claims Unobvious: Rebuttal of Alleged *Prima Facie* Case.....30

D. CONCLUSION..... 32

viii. CLAIMS APPENDIX 33

ix. EVIDENCE APPENDIX..... 42

x. RELATED PROCEEDINGS APPENDIX 49

TABLE OF AUTHORITIES

In Re Kahn, 441 F.3d 977, 985 (Fed. Cir. 2006) 11

KSR Int'l. Co. v. Teleflex Inc., 127 S. Ct. 1727 (2007)..... 11

In Re Oetiker, 088 F/2d 1443. 1445) Fed. Cir. 1988)..... 11

In Re Rijckaert, 9 F.3d 1531, 1532, 28 USPQ2d 1955, 1956 (Fed. Cir. 1993)..... 11

In Re Fine, 837 F.2d 1071, 1074, 5 USPQ2d 1596, 1598 (Fed. Cir. 1988) 11

In Re Nielson., 816 F.2d 1567, 1572, 2 USPQ2d 1525, 1528 (Fed. Cir. 1984) 12

In Re Gordon, 733 F.2d 900, 902, 221 USPW 1125, 1127 (Fed. Cir. 1984) 12

In Re Rouffet,, 149 F.3d 1350, 1355 (Fed. Cir. 1998)..... 12

MPEP §2143.....11

MPEP §2142.....12

MPEP §2145.....17

i. STATEMENT OF REAL PARTY IN INTEREST

The real party in interest in this appeal as of the filing date of this Appeal Brief is Bunge Oils, Inc..

ii. STATEMENT OF RELATED APPEALS AND INTERFERENCES

To the best of appellants' knowledge, there are no prior or pending appeals, interferences or judicial proceedings which will affect or be affected by or have a bearing on the Board's decision in this appeal.

iii. STATUS OF CLAIMS

Claims 1-5, 8, 9, 11-13, 15-17, 20-25, 27, 29, 37, 40, 41, 43, 44 and 46-48 are currently present in this application. Of these claims, claims 1, 37 and 40 are independent.

All of these claims are finally rejected, and all of such claims are being appealed. They are claims 1-5, 8, 9, 11-13, 15-17, 20-25, 27, 29, 37, 40 41, 43, 44 and 46-48.

iv. STATUS OF AMENDMENTS

Claims 1-48 were originally filed in this application. After an Office Action mailed February 2, 2007, several claims were amended in an Amendment of April 30, 2007.

After a Final Office Action mailed June 11, 2007, claims 10, 14, 26, 28, 30-34, 38, 39 and 42 were cancelled, and other claims were amended in an Amendment Under Rule 116 of September 11, 2007 and a second Final Office Action was mailed September 25, 2007, to which appellants responded on November 26, 2007 further amending independent claims 1, 37 and 40. After an Advisory Action mailed March 7, 2008, an RCE was filed March 17, 2008.

An Office Action mailed April 11, 2008 and its term was reset by a paper mailed June 18, 2008. An Amendment in response was filed on September 18, 2008, cancelling claims 6 and 45 and further amending independent claims 1, 37 and 40.

After another Final Office Action mailed December 3, 2008, independent claims 1, 37 and 40 were further amended and claims 7, 18, 19, 35 and 36 were cancelled in an Amendment After Final filed March 2, 2009, accompanied by a second RCE.

After an Office Action mailed April 9, 2009, an Amendment was filed July 31, 2009, amending independent claims 1, 37 and 40. A fourth Final Office Action was mailed October 21, 2009 to which appellants responded with an Amendment After Final filed January 18, 2010.

The fifth Final Office Action of March 24, 2010 is the action from which this appeal is taken, rejecting claims 1-5, 8, 11-13, 15-17, 20-25, 27, 29, 37, 40, 41, 43, 44 and 46-48. No claims are allowed or indicated to be allowable.

No amendments have been filed subsequent to the Final Office Action of March 24, 2010.

v. SUMMARY OF CLAIMED SUBJECT MATTER

In accordance with §41.37(c)(v), appellants are providing the following summary of claimed subject matter defined in each appealed independent claim by presenting a concise explanation thereof. Appellants provide examples of where the elements of the independent claims are shown or discussed in the specification and drawings in the original application. These citations are merely examples, as the application may have further disclosure of these elements throughout the application. Appellants understand none of the appealed claims are means or step plus function claims.

Independent claim 1 is directed to a liquid vegetable oil composition, independent claim 37 is directed to a method for making a health and nutrition promoting liquid vegetable oil composition, and independent claim 40 is directed to a method for using a medium chain triglyceride in a health and nutrition

promoting liquid oil composition. Each of independent claims 1, 37 and 40 specify, among other Features:

A. An interesterified liquid structured lipid component that is an all-vegetable component (**[0004]**, **[0007]**, **[0021]** and **[0026]** and original claims 18, 19, 35 and 36). Independent claims 1 and 37 state that this component comprises at least 88 weight percent of the composition (**[0043]** and original claims 1 and 21).

B. The interesterified structured lipid component is a randomization reaction product with interexchanged first and second fatty acid chains that vary randomly from glycerol structure to glycerol structure (**[0009]** and **[0029]**).

C. The first fatty acid chains are of medium chain triglycerides of caprylic triglyceride, capric triglyceride or combinations thereof (**[0021]** and original claims 18 and 35).

D. The second fatty acid chains are long chain (at least C16) domestic vegetable oil triglycerides of soybean oil, corn oil, cottonseed oil, canola oil, olive oil, peanut oil, safflower oil, sunflower oil, oil from grain plants, and combinations thereof (**[0026]** and original claims 19 and 36).

E. A phytosterol ester component is included in the composition at 2 to 12 weight percent, as specified in claims 1 and 40, or at 2 to 10 weight percent according to claim 37 (**[0036]** and **[0043]** and original claims 1, 2, 22, 37, 43 and 44).

F. The composition reduces cholesterol adsorption in individuals (claim 1); consumption of the composition reduces LDL cholesterol adsorption by an individual (claim 37); and administering the composition to an individual to reduce LDL cholesterol adsorption by the individual (claim 40) (**[0045]**, **[0046]**, **[0098]**-**[0102]** and Rudkowska et al. publication).

Feature F is directed to the health and nutrition promoting characteristics of appellants' claimed invention. The structured lipid component according to the invention, for example, the combination of Features A through D, when included as the major component of the claimed composition and methods, which also incorporate the phytosterol ester component as in Feature E, bring about enhanced phytosterol delivery, as illustrated in Example 15, paragraphs **[0098]** to **[0102]**. Appellants' invention is discussed in Rudkowska et al. published in 2006 as an Elsivier distribution, which is of record in the application, having been submitted with the Amendment of September 18, 2008 as non-prior art to provide test data

illustrating health promotion in terms of reducing cholesterol adsorption in individuals. This is included in the Evidence Appendix of this Brief.

vi. GROUNDS OF REJECTION TO BE REVIEWED

Claims 1-5, 8, 9, 11-13, 15-17, 20-25, 27, 29, 37, 40, 41, 43, 44 and 46-48 are rejected under 35 U.S.C. §103(a) using Aoyama (U.S. Patent No. 6,827,963) in view of Wester et al (U.S. Patent No. 6,589,588), 21 C.F.R. §101.83 and St.-Onge et al., "Consumption of a Functional Oil Rich in Phytosterols and Medium Chain Triglyceride Oil Improves Plasma Lipid Profiles in Men," *American Society for Nutritional Sciences*, 2003, taken together with Baileys Industrial Oil and Fat Products, pp. 54-55, 178-180, 192-196 and 210-212, John Wiley & Sons, Inc., 1979.

vii. ARGUMENT

THE REJECTION OF THE CLAIMS UNDER 35 U.S.C. §103 SHOULD BE REVERSED

A. The Law Regarding Obviousness

Under 35 U.S.C. §103(a), a claimed invention is unpatentable if the differences between it and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having

ordinary skill in the pertinent art. 35 U.S.C. § 103(a) (2000); *In re Kahn*, 441 F.3d 977, 985 (Fed. Cir. 2006). More recently, the U.S. Supreme Court addressed the proper steps and considerations for determining obviousness. *See KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727 (U.S. 2007). These steps include conducting certain factual inquiries and providing "articulated reasoning... to support a legal conclusion of obviousness." *See Id.* at 1741. While *KSR* has been recognized as a significant pronouncement on the law of obviousness, it did not revise the allocation of the burden of proof in Patent and Trademark Office proceedings.

Under 35 U.S.C. 103(a), the initial burden is on the PTO Examiners to produce evidence that the claimed invention is *prima facie* obvious. *In re Oetiker*, 977 F.2d 1443, 1445 (Fed. Cir. 1992); *In re Rijckaert*, 9 F.3d 1531, 1532, 28 USPQ2d 1955, 1956 (Fed. Cir. 1993); *In re Fine*, 837 F.2d 1071, 1074, 5 USPQ2d 1596, 1598 (Fed. Cir. 1988). To establish a *prima facie* case of obviousness, all of the claim limitations must be taught by the cited art, in such combination each element merely performs the same function as it does separately, one of ordinary skill would have recognized that the results from the combination were predictable, and whatever additional findings may be necessary to explain a conclusion of obviousness. MPEP § 2143, section A(1). If the PTO fails to make out a *prima facie* case of obviousness, then the rejection is improper, should be overturned, and Applicants are entitled to a patent. *Rijckaert*, 9 F.3d at 1532, 28 USPQ2d at 1956;

In re Nielson, 816 F.2d 1567, 1572, 2 USPQ2d 1525, 1528 (Fed. Cir. 1984); *In re Gordon*, 733 F.2d 900, 902, 221 USPQ 1125, 1127 (Fed. Cir. 1984).

As explained in MPEP §2142, the burden is initially on the Examiner to establish a *prima facie* case of obviousness. If the Examiner does not establish a *prima facie* case, then the rejection is improper and should be withdrawn. "On appeal to the Board, an applicant can overcome a rejection by showing insufficient evidence of *prima facie* obviousness..." *In re Kahn*, 441 F.3D 977, 985-86 (Fed. Cir. 2006) (*citing In re Rouffet*, 149 F.3d 1350, 1355 (Fed. Cir. 1998)). As will be explained below, in this case, the references do not teach or suggest all the limitations of appellants' claims. Therefore, no *prima facie* case of obviousness has been established.

Furthermore, as explained below, any case of alleged *prima facie* obviousness by the Examiner has clearly been rebutted by arguments and test data. Accordingly, all of the obviousness rejections of the claims must be reversed.

B. Claims Unobvious: The Multiple References Do Not Disclose All the Claimed Elements

1. *Claim 1 and its dependent Claims 2-5, 8, 9, 11-13, 20-25, 27 and 29:*

In the Final Office Action appealed from, the Examiner rejects these (and all other) claims as obvious from Aoyama (cited for the first time in the sixth Office Action) and the secondary references. This is in error for the following reasons.

(a) Aoyama and Product Claim 1

On page 3 of the Final Rejection appealed from, the Examiner acknowledges that Aoyama teaches directed interesterification to prepare triglycerides, such being recognized as being the case in all of the Aoyama examples and as reported in Aoyama. The Examiner references lines 18-23 in column 8 of Aoyama, about which the Examiner states: "The use of random or chemical interesterification is suggested."

Also on page 3 of the Final Rejection, the Examiner takes the position that the specific way appellants' synthesized triglyceride is made is a process limitation, carrying no weight in product claim 1. Appellants respectfully observe that claim 1 does recite its liquid structured lipid component in terms of chemical structure and not as only a process limitation. More specifically, claim 1 recites specific medium chain vegetable triglycerides, defining same as having first fatty acid chains. Similarly, claim 1 specifically recites a selection of long chain domestic vegetable oils, defining them as having second fatty acid chains of at least C16 in length. The specific medium chain triglycerides specified in claim 1 are much shorter in chain length, namely caprylic, which is C8, and capric, which is C10. Thus, claim 1 specifies first fatty acid chains having a chain length different from (substantially less than) the second fatty acid chains. Furthermore, the liquid structured lipid component is further identified in structural or product

terms as being a randomization reaction product having interchanged first and second fatty chains that vary randomly from glycerol structure to glycerol structure. In other words, while the liquid structured lipid component is referred to in claim 1 as a randomization reaction product, this product is also defined in product terms, namely having first and second (i.e., different) fatty acid chains that define the structured lipid component as having those different first and second chains on the glycerol structure in a random fashion.

Because of the nature of randomness, it is not possible to provide a specific structural formula, such as the Formulas of Aoyama. As noted elsewhere by appellants, this is a very important point of distinction between Aoyama, which is able to provide specific structural formulas for the directed interesterification products described in Aoyama. Instead of such formulations, appellants claim the structured lipid component as having randomly distributed on each glycerol structure the specifically defined first or second fatty acid chains.

Accordingly, Feature B identified in the Summary of Claimed Subject Matter provided earlier in this Brief carries weight in product claim 1 and is a feature that is not taught by Aoyama or any of the other references.

(b) <u>Aoyama and "a chemical synthesis method"</u>

Despite the fact that Aoyama does not teach Feature B, the Examiner, on page 5 of the Final Rejection appealed from, says that the statement at lines 19-23

in column 8 of Aoyama "contemplates random interesterification." Appellants understand this to mean that the Examiner takes the position that Aoyama intrinsically discloses triglycerides prepared by random interesterification where first and second (i.e., different) fatty acid chains vary randomly from glycerol structure to glycerol structure.

Appellants appreciate that lines 20-21 in column 8 of Aoyama recite the phrase "a chemical synthesis method." This is the one and only time Aoyama provides any disclosure or alleged teaching about "chemical synthesis" or randomization reaction products. It is of course very evident from Aoyama that any degree of Aoyama enablement or disclosure for ester preparation concerns only **the enzyme method** to prepare the Aoyama fats and oils composition. In addition to the phrase "a chemical synthesis method," this paragraph in column 8 of Aoyama also mentions "a method of extracting from natural fats and oils" as well as "a genetic recombination method of oil seeds." As with the "chemical synthesis" method, Aoyama provides no disclosure concerning these other two methods, other than to name them.

The secondary references to Wester, C.F.R., St.-Onge and Bailey do not concern interesterification and accordingly the focus of the present Brief concerns what one of ordinary skill in the art would have been taught by Aoyama without the benefit of appellants' disclosure and teaching. One of ordinary skill in the art

would need more guidance than the mere statement of "a chemical synthesis method," which is all that is provided by Aoyama. Aoyama does not enable one of ordinary skill in the art to make the compositions according to his invention by using "a chemical synthesis method." Of course, even if this were the case, the products and methods of the appealed claims are not present in Aoyama. The only enablement provided in Aoyama is making the Aoyama "fats and oils composition" by the enzyme method.

More to the point of appellants' claimed invention, Aoyama does not disclose or teach the appellants' liquid structured lipid component. Instead, Aoyama teaches driving the esterification to triglycerides in which specified fatty acids are combined so as to provide a specific acyl group at the first portion, a specific acyl group at the second portion and a specific acyl group at a third portion of the triglyceride molecule. Same are disclosed by Aoyama as "Formulas," namely Formula I, Formula II, Formula II', Formula III, Formula III', Formula IV, Formula V or Formula VI. Thus, Aoyama teaches glycerol backbones having fatty acids placed thereon at a specific position on the glycerol backbone, which would not have obviously led one of ordinary skill in the art to appellants' claimed invention.

The Examiner is relying on only the gratuitous phrase "a chemical synthesis method" in Column 8 of Aoyama. This phrase does not negate the fact that

Aoyama does not disclose the interesterified randomization invention specified in appellants' claims, either intrinsically or otherwise. Additionally, this one-time mention of "a chemical synthesis method" in column 8 of Aoyama would not have taught one of ordinary skill in the art to expect formation of appellants' invention. Furthermore, Aoyama does not even remotely enable one of ordinary skill in the art to achieve appellants' claimed invention. Appellants note that M.P.E.P. §2145 states:

> A conclusion of obviousness requires that the reference(s) relied upon be **enabling in that it put the public in possession of the claimed invention**. (citing *In re Hoeksema*, 399 F.2d 269, 274, 158 USPQ 596, 601 (CCPA 1968), bolding added.)

Aoyama's teachings and disclosure regarding using the enzyme method to drive the esterification toward the Aoyama compositions that Aoyama identifies as triglycerides of specific structures, namely the Formulas noted above, does not intrinsically result in or otherwise enable the interestified randomization liquid structured lipid component of appellants' claims.

Clearly, Aoyama does not disclose an interesterified randomization liquid structured lipid commensurate with the appealed claims. After a full and thorough reading of Aoyama, the Examiner and Board should appreciate that same is not even remotely adequate to prepare the invention of the present claims, namely a liquid structured lipid that is an interesterified randomization product with fatty

acid moiety chains from one glycerol randomly exchanged with fatty acid moiety chains from another, different glycerol, such liquid structured lipid having randomly esterified different fatty acid moiety chains that vary from glycerol structure to glycerol structure. Aoyama simply does not teach or enable the skilled esterification artisan about randomly interchanged liquid structured lipids of appellants' invention.

Appellants observe that Aoyama's totally unsupported and gratuitous phrase "a chemical synthesis method" does not come close to rising to the level of enablement for having "a chemical synthesis method" result in **Aoyama's own** "fats and oils composition" Formulas. This being the case, it is impossible for Aoyama to enable preparation of **appellants'** claimed products by "a chemical synthesis method" since same are not at all the subject of Aoyama and they are not described by Aoyama, intrinsically or otherwise.

The Board will appreciate, appellants respectfully believe, that Aoyama's use of the phrase "a chemical synthesis method" does not mean that appellants' structured lipids intrinsically are prepared by random interestification, even if Aoyama might use MCTs and long-chain lipids of appellants' claims as the reactants. This is because enzymes and chemical catalysts are very different from each other and would require much more than the simple statement "a chemical synthesis method" in order to intrinsically teach or enable preparation of a different

product (appellants' claimed invention versus Aoyama's Formulas) by a different means ("a chemical synthesis method" versus "the enzyme method"). It is well known in the art that enzyme reactions and chemical synthesis are very different from each other. Each reacts with substrates at different rates and with different selectivities based on many characteristics such as shape, size and electrostatic interactions. For example, enzymes are relatively complex large chemical structures, while chemicals of chemical syntheses are of a relatively small and simple chemical structure. The skilled artisan would need details of interesterification conditions, such as whether the chemical synthesis conditions are under an acidic or a basic condition. Of course, any such disclosure is absent from Aoyama.

Appellants respectfully assert that, since Aoyama provides absolutely no information on chemical interestification conditions, what chemicals would be used in "a chemical synthesis method" or anything else about chemical synthesis, and since these types of details are essential, Aoyama would not enable a skilled artisan to produce the claimed invention.

In summary, appellants urge reversal because of these quite evident shortcomings of Aoyama:

1. The skilled esterification artisan is not taught or enabled by Aoyama how to make the Aoyama "fats and oils composition" Formulas by "a chemical synthesis method."

2. To the extent the skilled esterification artisan would be taught anything by Aoyama by the stand-alone phrase "a chemical synthesis method" the teaching would be same would drive interesterification to or toward the Aoyama Formulas and not to or toward randomization as appellants claim.

3. The esterification artisan would not be enabled to achieve random interexchanging through interesterification by the simple statement in Aoyama of "a chemical synthesis method" inasmuch as Aoyama is devoid of any mention – let alone any specifics – of interesterification conditions for "a chemical synthesis method."

Thus Aoyama has significant shortcomings and deficiencies. Aoyama does not disclose all of Features A, B, C, D, E and F.

(c) The Secondary References

Concerning the secondary references, the paragraph common to pages 5 and 6 of the Final Office Action appealed from acknowledges that none of Wester, C.F.I., St.-Onge or Bailey are directed to random interesterification. The Examiner refers to St.-Onge, apparently taking the position that because St.-Onge does not

describe how he obtained his MCT oil, this somehow relates to a teaching of an MCT having undergone interesterification with a long chain domestic oil. The Examiner seeks to support this position by saying only that: "Ayoama contemplates even natural sources of MCT at column 8, lines 19-23."

St.-Onge mentions blends of medium chain triglyceride oil and phytosterols, without any suggestion that an MCT oil according to St.-Onge would have been or is to be interesterified – randomly or otherwise – with any other component, let alone with a long chain domestic oil as appellants claim. For example, the Abstract of St.-Onge states that the study of that publication evaluates the effects of a combination of MCT oil, phytosterols and flaxseed oil ("functional oil" or FctO) on plasma lipid concentrations and LDL particle size. The first paragraph of St.-Onge refers to medium chain triglycerides (MCT) and the effects thereof. Throughout St.-Onge, the reference is to "MCT" or "MCT oil." In the second paragraph on page 1816, St.-Onge reports that the dietary fat of the testing reported by this article was either "FctO or OL." The next paragraph states that FctO "was prepared by heating MCT oil and coconut oil and dissolving tall oil phytosterols ..." A footnote identifies FctO as functional oil and OL as olive oil. Thus, the fats of St.-Onge are either olive oil or a blend of MCT oil and another oil, such as flaxseed oil or coconut oil. Neither FctO nor OL is an interesterified structured lipid of appellants' claims. Table I of St.-Onge provides further information about

the FctO diets. Only MCT oil, cocoanut oil, canola oil and flaxseed oil are listed, no interesterified products being listed. Similarly, Table II shows the makeup of fatty acids in the FctO, again providing no suggestion that these concern anything but blends of fatty acid oil. The first paragraph of the Discussion section that begins on page 1818 of St.-Onge, in the very first sentence, refers to "a combination of MCT oil, phytosterols and flaxseed oil." Again, nothing about interesterification, random interesterification or esterification of any type. The very last sentence in this Discussion section of St.-Onge specifically refers to "an MCT-containing oil blend." **A blend is not an interesterification.**

With these observations and the statements made in the Final Rejection appealed from, appellants confidently reiterate their position that none of Wester, C.F.R., St.-Onge or Baileys are directed to random interesterification.

The Examiner relies upon **Wester** to address Aoyama's failure to disclose phytosterol esters. Wester is cited as teaching incorporation of phytosterol esters into specific foods including cooking oils to reduce serum cholesterol in the body by reducing the absorption of cholesterol from the digestive tract. Appellants do not claim phytosterols or their use as their invention. But appellants claim their composition of the claimed liquid structured lipid randomization interesterification component combined with the phytosterol ester component improves phytosterol delivery and reduces cholesterol adsorption in individuals. Because Wester has no

teaching concerning random interesterification or the liquid structured lipid components that are claimed by applicants and that are not taught or contemplated by Aoyama, Wester does not remove Aoyama's extensive deficiencies.

The Examiner relies on the **C.F.R.** reference for showing levels of phytosterol ester fortification required to make labeling claims with regard to lowering cholesterol and reducing coronary heart disease risk. This reference has no teaching concerning randomization interesterification or with appellants' claimed liquid structured lipid component having the randomly positioned first and second fatty acid chains or moieties.

The **St.-Onge** reference is cited for its teaching that oils rich in phytosterols and medium chain triglyceride oil are known to be improved by plasma lipid profiles. St.-Onge does not remove Aoyama's or Wester's or the C.F.R.'s deficiencies regarding the claimed randomized interesterified liquid structured lipids inventions claimed by appellants.

Bailey is relied upon by the Examiner in the Final Office Action appealed from with respect to properties of viscosity and smoke point and melting points of certain vegetable oils, not randomization interesterification lipids of the invention. Nor does Bailey teach any of these properties for interesterification products from any such vegetable oils.

(d) Appellants' Invention is Unobvious

For these reasons, with the combination of references posited by the Examiner in this Final Office Action – even if they had been obvious to combine – one of ordinary skill would not have arrived at all of Features A through F of appellants' invention of claims 1, 2-5, 8, 9, 11-13, 20-25, 27 and 29. Reversal of the §103 rejection is respectfully requested with respect to these claims.

Furthermore, even if the Board is of the opinion that a *prima facie* case has been made, the record shows same has been properly and successfully rebutted. Appellants refer the Board to section C. of this Brief which consolidates these points at a single location to facilitate their consideration.

2. Claim 15 (Dependent on Claim 1)

Claim 15 is dependent on claim 1, was not separately rejected in the Final Office Action, but is argued separately here. Neither Aoyama nor any of the secondary references would have obviously led to a liquid structured lipid composition that is a clear liquid and remains a clear liquid for at least six months when stored at 21° C. Table I, Table II and paragraphs **[0056]** to **[0064]** of the present application report tests that illustrate this feature, including oxidative stability being twice that of fresh canola oil. These data and paragraphs show the advantages of this feature of claim 15 by having an edible oil composition remain

stable and clear (paragraph **[0057]**) much longer than control oils such as canola oil.

3. Claim 16 (Dependent on Claim 1)

In the appealed-from Final Office Action, claim 16 was not separately rejected. This claim is directed to the feature that the oil composition has sensory attributes not significantly different from or significantly superior to corresponding sensory properties of canola oils that do not have a phytosterol component. This feature means that the phytosterol sensory properties are "masked," being at least as good as a premium edible oil, namely canola oil, that does not have any phytosterol blended into it. This feature is reported on and discussed in greater detail in multiple locations in the application as filed, including paragraphs **[0055]** and **[0056]**, as well as Table I of Example 1, and especially at paragraphs **[0069]**, **[0071]**, **[0073]**, **[0075]**, **[0077]**, **[0079]** and **[0082]**. Test results included in these passages establish this sensory feature improvement over canola oils known in the industry for their high-end attributes.

References such as Wester, C.F.R. and St.-Onge do not disclose that any of the edible oils discussed therein have this important sensory feature in relation to phytosterols. It would not have been obvious to modify these references by replacing edible oils, including those mentioned in St.-Onge, for example, with the

liquid structured lipid component of appellants' invention. For this reason, claim 16 is argued separately as unobvious.

4. Claim 17 (Dependent on Claim 1)

Claim 17 is dependent on claim 1 and was not separately rejected in the Final Office Action. This claim is directed to the feature that the oil composition has sensory attributes not significantly different from or significantly superior to corresponding sensory properties of olive oils that do not have a phytosterol component. This feature means that the phytosterol sensory properties are "masked," being at least as good as a premium edible oil, namely olive oil, that does not have any phytosterol blended into it. This feature is reported on and discussed in greater detail in multiple locations in the application as filed, including paragraphs **[0075]** and **[0084]**, as well as Table III of Example 1. Test results included in these passages establish this sensory feature improvement over olive oils known in the industry for their high-end attributes.

References such as Wester, C.F.R. and St.-Onge do not disclose that any of the edible oils discussed therein have this important sensory feature in relation to phytosterols. It would not have been obvious to modify these references by replacing edible oils, including those mentioned in St.-Onge, for example, with the

liquid structured lipid component of appellants' invention. For these reasons, claim 17 is argued separately as unobvious.

5. Claim 37 (Independent)

As noted in section vii.B.1.(a) of this Brief, on page 3 of the appealed-from Final Office Action, claim 1 is singled out as being a product claim and not entitled to benefit from the "specific way that the synthesized triglyceride is made," the Examiner stating same is "a process limitation." As noted in that section, appellants disagree with this position that is articulated by the Examiner. Appellants observe that, of course, this position was not taken by the Examiner with respect to independent claim 37, which is directed to a method for making a health and nutrition promoting liquid vegetable oil composition. Thus, claim 37 has the specific features of introducing the reactants that are specifically identified in claim 37 and interesterifying these reactants by randomization that interchanges fatty acid moieties to the interesterified liquid structured lipid component having interchanged first and second acid chains that vary randomly from glycerol structure to glycerol structure. Because the Examiner does not take the position that these features are to be given no weight in claim 37, the unobviousness of claim 37 is argued separately in this Brief for this specific reason. Specifically,

any concern about the inapplicability of such method step features is obviated by the fact that claim 37 is a method claim.

Furthermore, appellants' arguments made herein with respect to claim 1, in section vii.B.1. hereof, apply to this rejection of claim 37 as well. Claim 37 is not obvious from Aoyama in combination with the secondary references.

6. Independent Claim 40 and its Dependent Claims 41, 43, 44 and 46

Finally rejected independent claim 40 is directed to a method for using a medium chain triglyceride in health and nutrition promoting liquid oil compositions. Similar to claim 37, the comments made by the Examiner on page 3 of the Final Rejection appealed from concerning claim 1 and the alleged process limitation and the allegation of carrying no weight in a product claim, this position is not made with respect to method claim 40. As with claim 37, claim 40 includes specific method steps, one being interesterifying by randomization that interchanges fatty acid moieties and so forth. See the discussion herein with respect to claim 37 at section vii.B.5. of this Brief.

Furthermore, because claim 40 is a method of using, this includes an administering step that is not found in in claim 1 or claim 37. This administering step includes reducing LDL cholesterol adsorption by the individual to whom the

composition is administered. This is an unobvious and unexpected important result that is discussed more fully in section vii.C.

Because of this, appellants argue separately that claims 40, 41, 43, 44 and 46 are unobvious. Furthermore, appellants' arguments made herein with respect to claim 1, in section vii.B.1. hereof, apply to this rejection of claim 40 as well.

Furthermore, even if the Board is of the opinion that a *prima facie* case has been made, the record shows same has been properly and successfully rebutted. Appellants refer the Board to section vii.C. of this Brief which consolidates these points at a single location to facilitate their consideration.

7. Claim 47 (Dependent on Claim 40)

The rejection of claim 47 in this section of the Final Office Action is argued separately as to unobviousness. Please see discussion herein of claim 15 in section vii.B.2.

8. Claim 48 (Dependent on Claim 40)

The rejection of claim 48 in this section of the Final Office Action is argued separately as to unobviousness. Please see discussion hereinabove of claims 16 and 17 in sections vii.B.3. and vii.B.4., respectively.

C. Claims Unobvious: Rebuttal of Alleged *Prima Facie* Case

Applicants believe that the arguments presented above are fully responsive to the multiple §103 rejections of the Final Office Action based on Aoyama as the primary reference in combination with secondary references that are also discussed hereinabove. To the extent the Board believes that the Examiner nevertheless has made a *prima facie* obviousness presentation in any of the §103 rejections, appellants respectfully point to data in the application and in a publication of testing under appellants' invention (Rudkowska et al.) that show the advantages obtained when all of features A, B, C, D, E and F of the Summary of Claimed Subject Matter are present.

The Examiner says on page 6 of the Final Office Action appealed from there is no unobvious difference seen between the test results of appellants and the test results of St.-Onge. To the contrary, there is **an enhancement of half again the LDL cholesterol reduction** in appellants' data when compared with the St.-Onge data.

Appellants' claimed invention achieves an enhanced unexpected benefit when one compares the St.-Onge clinical study data with clinical testing using appellants' invention. This St.-Onge article reports data on reduction in LDL cholesterol of 14% when compared to the baseline. Data of the clinical study using applicants' claimed invention (2006 publication of Rudkowska et al. "Phytosterols

Mixed with Medium-chain Triglycerides and High-oleic Canola Oil Decrease Plasma Lips in Overweight Men," which applicants had filed in this application (and is in the Evidence Appendix) show a reduction in LDL cholesterol of 21% when compared with the baseline.

More particularly, the respective clinical studies are properly compared due to similarities in testing protocol. The 2006 Rudkowska publication (applicants' claimed composition and methods) and the 2003 St. Onge prior art relied upon each report on clinical testing of men having a body mass index of 25-31 kg/m^2. Twenty-three of these men completed the study using applicants' invention, while thirty men were in the study of the 2003 St.-Onge publication. Each study followed a randomized crossover type of test, and each delivered the phytosterol-containing component with the same isoenergetic meal protocol of 15% protein, 40% fat and 45% carbohydrates. In the 2006 clinical study according to applicants' claimed invention, blood samples were taken at days 1, 2, 41 and 42, whereas in the 2003 St.-Onge clinical study, blood samples were taken at days 1, 28 and 29. Each analyzed the blood samples and calculated LDL cholesterol using the Friedenwald formula.

The baseline LDL for applicants' invention was 3.95, same being reduced to the end point value of 3.12, **a reduction of 21%**. *See* data in the table on page 393 in the "Functional Oil" columns and the "LDL-C" rows. As reported in Table 3 on

page 1817 of the St.-Onge publication, the baseline for the functional oil (FctO) for LDL-C was 3.43, and the Endpoint was 2.96, **a reduction of 14%**. Thus, **there is a 7% greater baseline reduction with appellants' invention when compared with St.-Onge**. This is an enhancement of **half again the enhancement** reported for St.-Onge.

Accordingly, these data provide further strong support for the unobviousness of the presently claimed invention. Reversal of the §103 rejection is further believed to be in order for this additional reason.

D. Conclusion

Appellants request that the Final Rejection appealed from be reverseded in all respects for all claims.

Respectfully submitted,

/Raymond M. Mehler/
Raymond M. Mehler
Registration No. 26,306

COOK ALEX LTD.
200 West Adams Street
Suite 2850
Chicago, Illinois 60606
Fax: 312-236-8176
docket@cookalex.com

Customer No. 26568

August 14, 2010

viii. CLAIMS APPENDIX

Listing of Claims:

1. (rejected) A liquid vegetable oil composition, comprising:

at least about 88 weight percent, based on the total weight of the oil composition, of an interesterified liquid structured lipid component that displays a solids fat content that is substantially liquid at 10°C, said interesterified liquid structured lipid component being an all-vegetable component;

said liquid structured lipid component is a randomization reaction product by which fatty acid moieties are interchanged of an interesterification reactant charge, said reactant charge having between about 30 and about 60 weight percent, based upon the total weight of the charge, of a medium chain vegetable triglyceride having first fatty acid chains, reacted with between about 40 and about 70 weight percent, based upon the total weight of the charge, of a long chain domestic vegetable oil triglyceride having second fatty acid chains of at least C16 in length, said liquid structured lipid component being the randomization reaction product having interchanged said first fatty acid chains and said second fatty acid chains that vary randomly from glycerol structure to glycerol structure;

said medium chain triglyceride is selected from the group consisting of caprylic triglyceride, capric triglyceride, and combinations thereof, and wherein said domestic oil is selected from the group consisting of soybean oil, corn oil, cottonseed oil, canola oil, olive oil, peanut oil, safflower oil, sunflower oil, oil from grain plants, and combinations thereof;

between about 2 and about 12 weight percent, based on the total weight of the oil composition, of a phytosterol ester component;

said liquid structured lipid component has a Brookfield viscosity at 20°C of between about 20 and about 52 centipoise and a smoke point of at least about 195°C (at least about 383°F); and

said vegetable oil composition of liquid structured lipid and phytosterol ester component is a liquid oil composition that reduces cholesterol adsorption in individuals.

2. (rejected) The composition in accordance with claim 1, wherein said structured lipid component comprises at least about 90 weight percent of the oil composition, and said phytosterol ester component comprises up to about 10 weight percent of the oil composition, both based upon the total weight of the oil composition.

3. (rejected) The composition in accordance with claim 1, wherein said structured lipid component comprises at least about 92 weight percent of the oil composition, based upon the total weight of the oil composition.

4. (rejected) The composition in accordance with claim 1, wherein said structured lipid component comprises up to about 96 weight percent of the oil composition, based upon the total weight of the oil composition.

5. (rejected) The composition in accordance with claim 1, wherein said structured lipid component comprises between about 92 and about 94 weight percent of the oil composition, based upon the total weight of the oil composition.

6. (cancelled)

7. (cancelled)

8. (rejected) The composition in accordance with claim 1, wherein said medium chain triglyceride amount is between about 35 and about 55 weight percent of the interesterification charge, and the amount of the domestic oil is between about 45 and about 65 weight percent of the charge.

9. (rejected) The composition in accordance with claim 1, further including an edible carrier component administered to an individual at a level of at least about 0.4 grams of said oil composition per kilogram of body weight per day.

10. (cancelled)

11. (rejected) The composition in accordance with claim 1, wherein said structured lipid component has a smoke point of at least about 205°C (greater than about 400°F).

12. (rejected) The composition in accordance with claim 1, wherein said phytosterol ester component has no greater than about 20% by weight, based upon the total weight of the phytosterol ester component, of a phytosterol.

13. (rejected) The composition in accordance with claim 1, wherein said oil composition reduces total cholesterol adsorption in individuals.

14. (cancelled)

15. (rejected) The composition in accordance with claim 1, wherein said liquid oil composition is a clear liquid and remains a clear liquid for at least about six months of storage at about 21°C.

16. (rejected) The composition in accordance with claim 1, wherein said oil composition has sensory attributes which are not significantly different from, or are significantly superior to, corresponding sensory properties of canola oils which do not have a phytosterol component.

17. (rejected) The composition in accordance with claim 1, wherein said oil composition has sensory attributes which are not significantly different from, or are significantly superior to, corresponding sensory properties of olive oils which do not have a phytosterol component.

18. (cancelled)

19. (cancelled)

20. (rejected) The composition in accordance with claim 1, wherein said structured lipid component and said phytosterol ester component provide an oil composition which has a Brookfield viscosity at 20°C of between about 20 and about 52 centipoise.

21. (rejected) The composition in accordance with claim 1, wherein said structured lipid component comprises at least about 88 weight percent of the oil composition, based upon the total weight of the oil composition.

22. (rejected) The composition in accordance with claim 1, wherein said structured lipid component comprises up to about 98 weight percent of the oil composition, based upon the total weight of the oil composition.

23. (rejected) The composition in accordance with claim 1, wherein said structured lipid component of the composition comprises between about 90 and about 96 weight percent of the composition, based upon the total weight of the oil composition.

24. (rejected) The composition in accordance with claim 20, wherein said structured lipid component comprises between about 92 and about 94 weight percent of the composition, based upon the total weight of the oil composition.

25. (rejected) The composition in accordance with claim 20, wherein said medium chain triglyceride amount is between about 35 and about 55 weight percent of the interesterification charge, and the amount of the domestic oil is between about 45 and about 65 weight percent of the charge.

26. (cancelled)

27. (rejected) The composition in accordance with claim 20, wherein said structured lipid has a smoke point of at least about 205°C (greater than about 400°F).

28. (cancelled)

29. (rejected) The composition in accordance with claim 20, wherein said medium chain triglyceride amount is up to about 60 weight percent of the interesterification charge, and the amount of the domestic oil is at least about 40 weight percent of the charge.

Claims 30 to 36. (cancelled)

37. (rejected) A method for making a health and nutrition promoting liquid vegetable oil composition, comprising:

providing a medium chain vegetable oil having first fatty acid chains;

providing domestic vegetable oil triglyceride having second fatty acid chains that have carbon chain lengths of between C16 and C22;

introducing a reactant charge to a reaction location, the reactant charge including between about 30 and about 60 weight percent of the medium chain vegetable oil triacylglyceride and between about 40 and about 70 weight percent of said domestic vegetable oil triglyceride, based upon the total weight of the reactant charge, said medium chain triglyceride is selected from the group consisting of caprylic triglyceride, capric triglyceride, and combinations thereof, and wherein said domestic oil is selected from the group consisting of soybean oil, corn oil, cottonseed oil, canola oil, olive oil, peanut oil, safflower oil, sunflower oil, oil from grain plants, and combinations thereof;

interesterifing by randomization that interchanges fatty acid moieties of said reactant charge into an interesterified liquid structured lipid component that is a randomization reaction product having interchanged said first acid chains and said second fatty acid chains that vary randomly from glycerol structure to glycerol structure, is an all-vegetable component and displays a solids fat content that is substantially liquid at 10°C; and

combining said all-vegetable interesterified liquid structured lipid component with a phytosterol ester component to provide an oil composition which is consumable by an individual and which promotes health and nutrition of that individual by reducing LDL cholesterol adsorption by the individual, said combining being such that the oil composition is a liquid oil composition that has a Brookfield viscosity at 20°C of between about 20 and about 52 centipoise has a smoke point of at least about 195°C (at least about 383°F), and contains at least about 88 weight percent structured lipid component and between about 2 and about 10 weight percent phytosterol ester component, based on the total weight of the oil composition.

38. (cancelled)

39. (cancelled)

40. (rejected) A method for using a medium chain triglyceride in a health and nutrition promoting liquid oil composition, comprising:

providing a medium chain vegetable oil triglyceride having first fatty acid chains;

providing domestic vegetable oil triglyceride having second fatty acid chains that have carbon chain lengths of between C16 and C22;

introducing a reactant charge to a reaction location, the reactant charge including between about 30 and about 60 weight percent of the medium chain vegetable oil triglyceride and between about 40 and about 70 weight percent of said domestic vegetable oil triglyceride, based upon the total weight of the reactant charge, said medium chain triglyceride is selected from the group consisting of caprylic triglyceride, capric triglyceride, and combinations thereof, and wherein said domestic oil is selected from the group consisting of soybean oil, corn oil,

cottonseed oil, canola oil, olive oil, peanut oil, safflower oil, sunflower oil, oil from grain plants, and combinations thereof;

interesterifing by randomization that interchanges fatty acid moieties of said reactant charge into an interesterified liquid structured lipid component that is a randomization reaction product having interchanged said first fatty acid chains and said second fatty acid chains that vary randomly from glycerol structure to glycerol structure, is an all-vegetable component and displays a solids fat content that is substantially liquid at 10°C;

combining said all-vegetable interesterified liquid structured lipid component with a phytosterol ester component to provide a health and nutrition promoting composition that is a liquid oil composition having between about 2 and about 12 weight percent of the phytosterol ester component, having a smoke point of at least about 195°C (at least about 383°F), and having a Brookfield viscosity at 20°C of between about 20 and about 52 centipoise; and

administering the composition to an individual in order to promote the health and nutrition of that individual by reducing LDL cholesterol adsorption by the individual.

41. (rejected) The method in accordance with claim 40, wherein said liquid oil composition has a smoke point of at least about 205°C (greater than about 400°F).

42. (cancelled)

43. (rejected) The method in accordance with claim 40, comprising combining at least about 88 weight percent of the structured lipid component, based upon the total weight of the composition, with the phytosterol ester component.

44. (rejected) The method in accordance with claim 40, comprising combining at least about 90 weight percent of the structured lipid component and up to about 10 weight percent of the phytosterol component, both based upon the total weight of the oil composition.

45. (cancelled)

46. (rejected) The method in accordance with claim 40, wherein said administering is at a level of at least about 0.4 grams of said oil composition per kilogram of body weight of the individual.

47. (rejected) The method in accordance with claim 40, wherein said oil composition is a clear liquid and remains a clear liquid for at least about six months of storage at about 21°C.

48. (rejected) The method in accordance with claim 40, wherein said oil composition has sensory attributes which are not significantly different from, or are significantly superior to, corresponding sensory properties of canola oils or olive oils which do not have a phytosterol component.

ix. EVIDENCE APPENDIX

Exhibit A: Rudkowska et al., "Phytosterols mixed with Medium Chain Triglycerides and High-Oleic Canola Oil Decrease Plasma Lipids in Overweight Men," *Metabolism Clinical and Experimental 55* (2006) 391-395, as reported in Elsevier Inc., 2006.

This publication was filed by appellants with the Amendment of September 18, 2008 and referred to in that Amendment, on page 3 of the Examiner's Final Office Action of December 3, 2008, on pages 15-17 of appellants' Amendment After Final of March 2, 2009, on pages 12-13 of appellants' Amendment of July 31, 2009, on page 6 of the Examiner's Final Office Action of October 21, 2009, on pages 13-15 of appellants' Amendment After Final of January 18, 2010 and on page 6 of the Final Office Action under appeal.

EXHIBIT A
OF EVIDENCE APPENDIX

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Metabolism Clinical and Experimental 55 (2006) 391–395

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Phytosterols mixed with medium-chain triglycerides and high-oleic canola oil decrease plasma lipids in overweight men

Iwona Rudkowska[a], Catherine E. Roynette[a], Dilip K. Nakhasi[b], Peter J.H. Jones[a,*]

[a]School of Dietetics and Human Nutrition, Faculty of Agricultural and Environmental Sciences, McGill University, Montreal, Québec, Canada H9X 3V9
[b]New Product Development-NBD, Bunge Oils, Bradley, IL 60915, USA

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Abstract

Phytosterols (PSs) have been recently added to various mediums. Nevertheless, matrices with functional properties, such as medium-chain triglycerides (MCTs), should be precisely examined for supplementary advantages. The objective of this study was to identify the existence of combined biological actions of a functional oil enriched in PSs within MCTs and high-oleic canola (HOC), relative to a control (olive oil), in overweight, hyperlipidemic men using a rigorously controlled dietary intervention. Twenty-three overweight, hyperlipidemic men consumed both types of oil in a randomized, crossover trial for 6 weeks each. Fasted plasma samples were collected on the first and last 2 days of each study period. Body weight decreased -1.22 ± 0.35 kg ($P = .0019$) and -1.68 ± 0.47 kg ($P = .0016$) after the 6-week study period in the olive oil and functional oil groups, respectively. The end points for total cholesterol and low-density lipoprotein cholesterol (LDL-C) in the functional oil group ($P = .0006$) were lower than in the olive oil group ($P = .0002$). Total cholesterol values decreased from comparable baseline to end point of 4.71 ± 0.16 mmol/L ($P < .0001$) in the functional oil phase and 5.14 ± 0.19 mmol/L ($P = .0001$) in the olive oil phase ($P = .0592$). In addition, LDL-C demonstrated a similar drop, to an end point of 3.12 ± 0.16 mmol/L ($P < .0001$) and 3.54 ± 0.18 mmol/L ($P = .0002$), for the functional oil and olive oil groups, respectively, with significant changes ($P = .0221$). High-density lipoprotein cholesterol levels did not change in either treatment. Triacylglycerol end points decreased in functional oil and olive oil groups ($P = .0195$ and .0105, respectively) to the same extent from baseline. Results indicate that PSs mixed within an MCT- and HOC-rich matrix lower plasma LDL-C, without significantly changing the high-density lipoprotein cholesterol concentrations, in hyperlipidemic, overweight men, and may therefore decrease the risk of cardiovascular events.

1. Introduction

Numerous trials have established the ability of plant sterols (PSs) to reduce total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-C) [1]. In addition, high-density lipoprotein cholesterol (HDL-C) and triacylglycerol (TG) concentrations remained unaltered [1]. Plant sterols should be consumed with a meal to stimulate biliary flow to obtain an optimal LDL-C–lowering effect, and, indeed, various types of food vehicles can be used [2]. Plant sterols are generally given in a fat medium because this increases PS solubility and improves its consumption [1-4]. Most studies have used margarines and mayonnaise sources of PS [1-4]; however, other fat sources, especially those with functional properties, should be considered.

A potential oil to blend PSs with would be medium-chain triglyceride (MCT) oil. It has been shown to induce beneficial increases in energy expenditure and decreases in body fat [5-9] and thus potentially help reduce obesity. In addition, an experiment demonstrated that PSs in an MCT matrix could reduce TC more than PSs in a conventional oil containing long-chain triglycerides [10]. Although there are concerns regarding hypertriglyceridemic effects of MCT [11,12], 2 studies [13,14] used MCT in obesity prevention, blended with PS for their hypocholesterolemic properties, and demonstrated favorable effects on blood lipids concentrations.

Another possibility of a novel matrix could be an oleic acid–rich oil, given that it may be beneficial for the prevention of hyperlipidemia through lowering both TC and TG concentrations. Therefore, we hypothesized that the consumption of PSs in a mixture of MCT oil and high-oleic canola (HOC) oil would prevent undesirable increases in blood lipid concentrations. The objective of this study

* Corresponding author. Tel.: +1 514 398 7841; fax: +1 514 398 7739.
E-mail address: peter.jones@mcgill.ca (P.J.H. Jones).

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Table 1
Macronutrient composition of the study diet (12552 kJ/d)

Composition	Protein (% energy)	Carbohydrates (% energy)	Fat (% energy)	Fiber (g)
Day 1				
Breakfast	4.6	16.5	13.7	9
Lunch	3.9	14.4	11.8	6
Supper	4.8	16.2	14.1	8
Total % energy	13.3	47.1	39.6	23
Day 2				
Breakfast	3.8	18.3	13.2	4
Lunch	2.7	14.9	12.0	7
Supper	4.4	16.6	14.1	11
Total % energy	10.9	49.8	39.3	22
Day 3				
Breakfast	4.9	16.6	13.3	4
Lunch	4.5	14.0	12.7	10
Supper	4.8	16.2	13.0	10
Total % energy	14.2	46.8	39.0	24

was therefore to identify the existence of combined biological actions of a functional oil enriched in PSs within MCTs and HOC, relative to a control oil in overweight, hypercholesterolemic men using a rigorously controlled dietary intervention.

2. Subjects and methods

2.1. Subjects

Thirty-two hyperlipidemic, overweight men were recruited from the surrounding community of Montreal through newspaper advertising. Subjects were 18 to 45 years of age, with a body mass index between 25 and 33 kg/m^2 and plasma LDL-C of more than 3 mmol/L. Before enrollment, subjects were required to provide a medical history and to undergo a complete physical examination. Subjects were excluded if they had used oral hypolipidemic therapy or had diabetes, hypertension, hypothyroidism, or other known metabolic disorders. Fasting blood samples were collected for serum biochemistry and hematology to test LDL-C levels and normality of other parameters. Before study entry, subjects received a complete description of the protocol, and informed consent was obtained from participants. The study protocol was reviewed and accepted by the Human Ethical Review Committee of the Faculty of Agriculture and Environmental Sciences of McGill University.

2.2. Experimental design and diets

A randomized, single-blind, crossover study consisting of 2 independent phases of 6 weeks each and an intermediary washout period of 4 to 8 weeks was conducted. The experimental diets consisted of prepared meals, which were precisely weighed by the kitchen staff at the Mary Emily Nutrition Clinical Research Unit of McGill University. Diets were based on a 3-day rotating menu. Subjects were required to consume at least 1 of the 3 meals at the clinic under supervision of the clinical staff. Diets were served as 3 isoenergetic meals per day (Table 1) and provided ~45% of energy as carbohydrates, ~15% as protein, and ~40% as fat, of which 75% was delivered as treatment fat. The remaining 25% of total fat was found in the standard food items, identical in both diets. Treatment fat, either as functional or control oil, was directly incorporated. The control oil, extra-virgin olive oil, was included into the meals to improve participants' blinding. The functional oil (Delta SL, Bunge North America) consisted of 3 major components: 45% to 47% HOC interesterified with 45% to 47% MCTs, and 6% to 10% of sterol esters were physically blended in after the interesterification. Each meal contained comparable amounts of fat derived from the test oil. Nonfat and nonsterol constituents were identical across diets. The nutrient intake of the diet was adjusted to tailor each individual's specific energy requirements using the equation of Mifflin et al [15] to control energy balance, to which an activity factor of 1.7 was added to compensate for energy expended in physical activity (PA). Patients were asked to maintain a constant level of PA throughout the entire study; however, the direct energy cost of PA was not measured. The different energy densities of MCT and long-chain triglyceride, 34 and 38 kJ/g, respectively, were accounted for in the calculation of energy intake to ensure that functional and extra-virgin olive oil diets were isoenergetic. During the first week of phase 1, energy intake was readjusted to correct energy balance. Energy intake was fixed thereafter and was identical during both dietary phases. Body weight was monitored daily upon arrival at the clinic. No extra food was allowed between meals except for decaffeinated, energy-free carbonated beverages, and herbal teas, which were provided by the clinic. The nutrient content of the diets was determined using Food Processor (ESHA Research, Salem, OR).

2.3. Plasma analyses

Blood samples were collected after an overnight fast on days 1, 2, 41, and 42 of each experimental phase. Samples were collected in duplicate to decrease the day-to-day variability. Blood samples were then centrifuged at 1500 rpm for 20 to 25 minutes, and plasma, serum, and red blood cells were immediately separated into 0.5- to 1-mL aliquots and stored at −20°C for future analysis. Plasma lipid aliquots were sent to and analyzed at the Lachine Clinic (Montreal, Canada). An enzymatic colorimetric test (enzymatic kit, Roche Diagnostics, Indianapolis, IN) was used for TC and TG [16,17]. The TC determination was based on Δ^4-cholestenone after enzymatic cleavage of the cholesterol ester by cholesterol esterase, conversion of cholesterol by cholesterol oxidase, and subsequent measurement by the Trinder reaction of the hydrogen peroxide formed [18]. This determination is based on the work by Roeschlau et al [16], using a lipoprotein lipase derived from microorganisms.

Table 2
Changes in blood lipids in hypercholesterolemic men after 6 weeks of consuming diets rich in either olive or functional oil

	Olive oil (n = 23)				Functional oil (n = 23)				Between-group P	
	Baseline	±SEM	End point	±SEM	Baseline	±SEM	End point	±SEM	Baseline P	End point P
Weight										
Average	86.34	2.38	85.12	2.36	86.33	2.21	84.65	2.20	.9875	.3477
Difference			1.22	0.35			1.68	0.47		.2123
TC										
Average	5.73	0.18	5.14	0.19	5.68	0.21	4.71	0.16	.7075	.0006[a]
Difference			0.60	0.13			0.97	0.17		.0592
LDL-C										
Average	4.00	0.18	3.54	0.18	3.95	0.19	3.12	0.16	.6917	.0002[a]
Difference			0.46	0.1			0.83	0.15		.0221[a]
HDL-C										
Average	0.97	0.07	0.93	0.04	0.91	0.04	0.89	0.03	.1063	.1533
Difference			0.04	0.04			0.02	0.02		.3607
TG										
Average	1.69	0.15	1.48	0.13	1.81	0.14	1.53	0.11	.2170	.4309
Difference			0.22	0.09			0.27	0.10		.6254

[a] Significant differences observed.

Determination of HDL-C in plasma was done using polyethylene glycol–modified enzymes and the dextran sulfate technique [19]. The low-density lipoprotein subfraction was indirectly quantified using the equation by Friedewald et al [20].

2.4. Statistics

Descriptive analysis of the data was expressed as mean ± SEM. Data for blood lipid concentrations for each phase were analyzed using a paired *t* test to determine significant changes between baseline and end point. An unpaired *t* test was used to establish differences between the 2 diets at baseline and at end point. The data were merged for analysis on SAS statistical software (SAS Institute, Cary, NC). $P < .05$ was used to determine significance.

3. Results

Thirty-three subjects were recruited; however, only 23 subjects completed the study. Five subjects dropped out during the first phase because of medical problems not related to the study (n = 1), because they disliked the meals (n = 2), or the time commitment required for the study (n = 2). In the second phase, additional subjects dropped out because of transportation problems (n = 4) and personal problems (n = 1). The 28% dropout rate was seen because of the lengthy and intensive study protocol. Subjects were young (mean age, 37 years), overweight (mean body mass index, 28 kg/m^2), hyperlipidemic men. All individuals tolerated the diet without any reported adverse events. Subjects could not differentiate between the oils.

The weights of the subjects at baseline, the average of the first 2 days, were similar for both oils (Table 2). Both the functional and control oil groups lost weight (−1.68 ± 0.47 kg, $P = .0016$; −1.22 ± 0.35 kg, $P = .0019$, respectively) after 6 weeks.

The end point for TC after functional oil feeding was lower ($P = .0006$) than that after the control oil phase, whereas the baseline TC data of 2 groups were not different ($P = .7075$) (Table 2). The TC values decreased ($P < .0001$) from 5.68 ± 0.21 to 4.71 ± 0.16 mmol/L, baseline to end point; therefore, a −17.0% change in the functional oil phase. A similar development was seen ($P = .0001$) with the control oil from 5.73 ± 0.18 mmol/L at baseline to 5.14 ± 0.19 mmol/L at end point, but this was to a lesser extent (−10.4%). Functional oil consumption resulted in 9.5% lower ($P = .0002$) LDL-C concentrations compared with control oil, although the baseline values for control oil and functional oil were similar ($P = .6917$). Low-density lipoprotein cholesterol concentrations decreased ($P < .0001$) from baseline 3.95 ± 0.19 mmol/L to end point 3.12 ± 0.16 mmol/L by −21.0% with the functional oil. The control oil also showed a decrease ($P = .0002$) from 4.00 ± 0.18 to 3.54 ± 0.18 mmol/L, a change of −11.5% in LDL-C. The magnitude of changes of TC did not differ between oils ($P = 0.0592$); however, LDL-C changes were statistically different ($P = .0221$). Values for high-density lipoprotein did not exhibit statistically significant difference in baseline ($P = .1063$) and end points ($P = .1533$) in the functional oil group compared with the control oil group. Triacylglycerol values decreased significantly during consumption of functional oil ($P = .0195$) and olive oil ($P = .0105$) from baseline. However, there were no differences seen between the baseline ($P = .2170$) and end point ($P = .4309$) data for TG values for functional oil vs control oil.

4. Discussion

Results from this study suggest that a functional oil containing PSs within an MCT and HOC mixture provides an effective means of favorably modulating blood lipid profiles in overweight, hypercholesterolemic men.

Functional oil contained 1.3 g/4184 kJ/d of diet of PSs mixed with MCT and HOC oil, in a high-fat diet over 6 weeks. Published results [1-3] indicate that addition of 1.5 to 3 g/d of PSs to the diet causes a 7% to 16% decrease in TC and an 8% to 15% reduction in LDL-C concentrations. Studies have shown that consuming higher doses of PS does not necessarily produce larger LDL-C–lowering effects [21]. An above-average decrease in TC and LDL-C concentrations in functional oil was probably due to the fact that diets were strictly controlled in conjunction with a high rate of compliance of participants in a suitable matrix. Oil-based products enriched with PS have shown to lower TC and LDL-C; however, oils with functional properties such as MCT have often been overlooked.

The MCTs that were included in the mixture may provide a further benefit of increased energy expenditure, thus potentially assisting in weight loss. This property of MCTs is thought to be mainly due to the fact that they are metabolized differently in comparison to long-chain triglycerides. Medium-chain triglycerides undergo direct transport to the liver via the portal vein, then are oxidized for energy, whereas long-chain triglycerides are absorbed by the intestinal lymphatic ducts and transported, as chylomicrons, through the thoracic duct, to reach the systemic circulation. Several studies report that MCTs are cholesterol neutral [22,23]; however, others reported hypercholesterolemic effects of MCT [12,24] because of high saturated fat content. Nevertheless, the functional oil in the present study did not increase TC and LDL-C, but on the contrary decreased concentrations. A recent study concluded that mixed micelles containing MCT lipolysis products have a reduced solubilizing capacity for cholesterol, therefore amplifying the effectiveness of PSs in displacing cholesterol [10]. This property enhances the benefits of MCT in cholesterol-lowering PS products. In addition, previous studies on similar functional oil formulations [13,14] have shown comparable results. First, Bourque et al [13] examined the effect of a diet supplemented with a functional oil composed of MCTs (50% of fat), PSs (22 mg/kg body weight), and n-3 fatty acids (5% of fat) in overweight women. The results demonstrated a significant reduction in mean plasma TC concentration by 9.1%. Low-density lipoprotein cholesterol was also significantly lower by 16% on functional oil. Subsequently, St-Onge et al [14] evaluated the effects of a similar functional oil as Bourque et al in normolipidemic, overweight men for 4 weeks compared with olive oil. The TC and LDL-C concentrations decreased significantly by 12.5% and 13.9% when subjects consumed functional oil, respectively, compared with 4.7% and no change for olive oil, respectively [14]. The difference in comparison to our study is the magnitude of changes for TC and LDL-C in functional oil and olive oil, which were higher in the present study. This might be due to the different type of population used, men vs women, normolipidemic vs hyperlipidemic, and the different doses of MCTs and PSs used in formulations. In addition, the current study was 6 vs 4 weeks [13,14]; the longer time might have further promoted the efficacy of PS in reducing blood lipid concentrations of subjects. Consequently, it can be inferred that the dose of PS of 1.3 g/4184 kJ/d in an MCT and HOC mixture was successful in optimizing TC reduction, including LDL-C lowering in hyperlipidemic, overweight men.

Triacylglycerol concentrations decreased similarly after feeding both the PS-containing functional oil and olive oil, indicative perhaps of the general characteristics of the diet provided by the clinic, as observed in past studies of a similar design [4]. The low simple sugar, alcohol-free, regular 3 meals per day cycle with reduced caffeine intake likely played an additional role in lowering circulating TG concentrations. In addition, previous research has shown that monounsaturated fatty acid–rich diets are associated with improvements in various endothelial functions and may have favorably affected TG concentrations in both control oil and functional oil groups. Furthermore, PSs have been shown not to affect TG concentrations [2]. Reduction of TG in the functional oil group addresses the question concerning MCT tendency to raise blood TG in humans [11] and shows that hypertriglyceridemia did not occur with the functional oil formulation. However, in a previous study on humans, the amount of MCTs consumed in test diets was higher than that in the present study. On the contrary, some reports have reported unchanged TG concentrations after MCT feeding [22,23,25]. In the current study, TG concentrations decreased in the functional oil group to an equal extent as observed in the control group, which might be due to the TG-suppressing effect modulated by other components such as the HOC or the lack of MCT-raising effect of TG.

Other factors may have contributed to the observed blood lipid changes, including the fact that the test diet fed was generally higher in fiber content (23 g/d); subjects subsequently lost weight during the trial. The absolute changes in weight after 6 weeks were not significantly different between the 2 oils; therefore, weight loss was not likely a factor on lipid concentration differences. Finally, the PA of subjects was not measured in the study; however, it can be assumed that there were no differences because HDL-C did not vary for either control or functional oil.

In summary, a functional oil mixture of PS in MCT and HOC demonstrated beneficial effects on plasma lipids by substantially lowering TC and LDL-C concentrations in comparison to a more conventional olive oil. Functional foods, which have added benefits over and beyond their basic nutritional value, such as the present oil, could contribute to a management strategy for hyperlipidemia.

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x. RELATED PROCEEDINGS APPENDIX

None